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DABCO-Catalyzed consecutive one pot four-component protocol for the synthesis of a novel class of (Z)-5-(3-hydroxy-2-oxoindolin-3-yl)-2-iminothiazolidin-4-ones

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Abstract. DABCO catalyzed, a novel and efficient one-pot, four component protocol has been developed for the synthesis of (Z)-5-(3-hydroxy-2-oxoindolin-3-yl)-2-iminothiazolidin-4-one scaffolds under metal-free conditions. By virtue of simple and readily available starting materials, mild reaction conditions, and the high bioactivity of oxindole derivatives, this reaction promises diverse applications in medical chemistry.

Oxindoles bearing a quaternary stereogenic center at C-3 are privileged heterocyclic motifs which exists in a vast array of natural products and biologically active molecules such as maremycins A and B,[1a] convolutamydines A-E,[1b] arundaphine,[1c] dioxibrassinine,[1d,1e] donaxaridine, welwitindolinone C,[2a] diazonamide A,[2b] leptosin D,[2c] elogentin K,[2d] neuroprotectins,[2e] and CPC-1.[2f] In particular, 3-functionalized-3-hydroxy-2-oxindoles are known to possess a broad spectrum of biological activities such as anti-inflammatory, antiviral, anticonvulsant, anti-HIV, antidepressant, antimicrobial, as well as they are potential new targets for chemotherapy (Fig. 1).[3] For example, SM-130686 has been identified as a potent growth hormone secretagogue,[4a] whereas compound **F** in Fig. 1 showed improved anti-HIV properties than FDA-approved NNRTI drug efavirenz.[4b]

Additionally, five-membered heterocyclic ring containing thiazolidinone moiety plays an important role in the area of medicinal chemistry with diverse biological activities such as antimicrobial,[5a,b] antidiarrheal,[5c] anticonvulsant,[5d-f] antibacterial,[5g] antidiabetic,[5h] antihistaminic,[6a,b] anticancer,[6c] antifungal,[6d] and anti-HIV.[6e] Especially, 2-iminothiazolidin-4-one scaffolds have been found to possess significant pharmacological activities[7] as well as therapeutics,[8] fungicides and herbicides.[9]

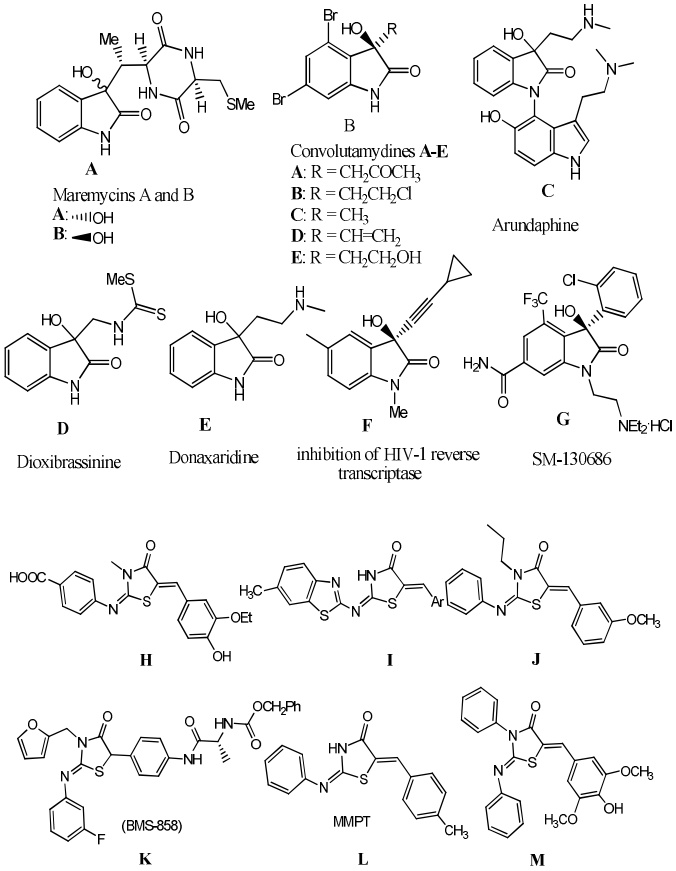

Figure 1: Selected representative examples of natural products and pharmaceuticals possessing 3-functionalized-3-hydroxy-2-oxindoles and some thiazolidinone derivatives with anticancer activity.

For example, 2-heteroarylimino-1,3-thiazolidin-4-ones were possess antifungal or antibacterial properties,[10] whereas darbufelone has

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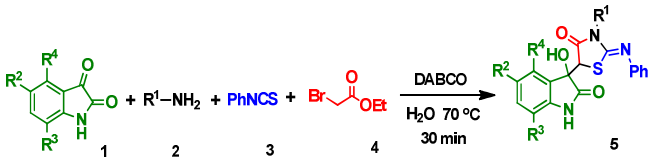
reported anti-inflammatory activity.[11] Imino-1,3-thiazolidin-4-one based derivatives compound **H** and **I** (Fig. 1) have been identified as potential anticancer agents.[12] Compound **K** (BMS-858) (Fig. 2) recognized as a specific inhibitor of hepatitis C virus (HCV) replication in a genotype 1b replicon and showed no significant inhibitory activity in counter screens.[13] Additionally, functionalized 2-Imino-5-arylidenethiazolidin-4-one **M** used as an inhibitor of bacterial type III secretion system.[14]

Structure–activity relationship studies have shown that the biological and pharmacological activities of these scaffolds vary with substitution on C-3 position of oxindoles and C-5 position of the thiazolidinone frameworks.[15] Hence it is thought of interest to accommodate oxindoles as well as iminothiazolidinones in a single molecular framework, which may result in the formation of some worthwhile molecules from a biological interest.

Multicomponent reactions (MCRs) have received much attention due to their wide range of applications in the organic, combinatorial, and medicinal chemistry for the rapid construction of novel and diverse molecular skeletons.[16] The strategy offers outstanding features such as one-pot operation, single step, higher efficiency, operation simplicity, result in both atom and step-economy.[17] MCRs can dramatically reduce chemical waste, energy, labor, time, cost, by-products formation, and provides an eco-friendly protocol by avoiding costly isolation and purification of intermediates.[18] Due to these advantages, the design of novel multicomponent reactions has been considered as biological interest.



R^1 = Butyl, Benzyl, Cyclopropyl, Ethyl; R^2 = H, F, Cl, Br, I, CH_3, OCH_3, OCF_3, R^3 = H, Cl, CH_3; R^4 = H, Cl.

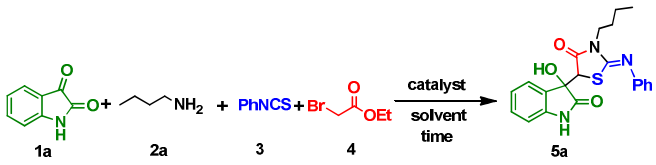
Scheme 1: Synthesis of (Z)-5-(3-hydroxy-2-oxoindolin-3-yl)-2-iminothiazolidin-4-one derivatives

Tertiary amines (non-metallic bases) are the example of a privileged catalyst class. Particularly, DABCO (1,4-diazabicyclo[2,2,2]octane) has emerged as an efficient organic-hindered base which has been successfully used for various organic transformations like deprotection of peptides,[19a] benzylictrimethylsilyl ethers,[19b] cyclization of o-alkynylaryl isocyanides,[19c] as a catalyst for the Baylis–Hillman reaction,[19d-f] cross-coupling reactions,[19g] o-alkylations of phenols,[19h] and synthesis of glycidic amidester.[19i] Additionally, DABCO is commercially available, non-toxic, and inexpensive reagent that can be used without special precautions. As for literature there is no method reported for the synthesis of new (z)-5-(3-hydroxy-2-oxoindolin-3-yl)-2-iminothiazolidin-4-ones using these current substrates. In continuation of our research work[20] on the synthesis of 3-substituted-3-hydroxy-2-oxindole frameworks, we wish to report a one pot four component protocol for the synthesis of a novel class of functionalized (z)-5-(3-hydroxy-2-oxoindolin-3-yl)-2-iminothiazolidin-4-ones by the reaction of substituted isatins, phenylisothiocyanate, ethylbromoacetate, and amines with DABCO in aqueous medium.

Results and discussions:

Our optimization studies began by examination of reaction parameters which included catalyst, solvent and temperature for the modal product (Z)-3-butyl-5-(3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one **5a**. The results are summarized in Table 1. Initially, we treated simple isatin, phenylisothiocyanate, ethylbromoacetate and butylamine in the presence of 10 mo1% DBU in 5 mL of H_2O at 70 °C. We obtained the solid product in 55% yield only even after 1 h. The structure of obtained product was confirmed by means of ^1H NMR, ^{13}C NMR, IR and Mass spectrometry analysis.

Table 1: optimization of reaction condition[a]



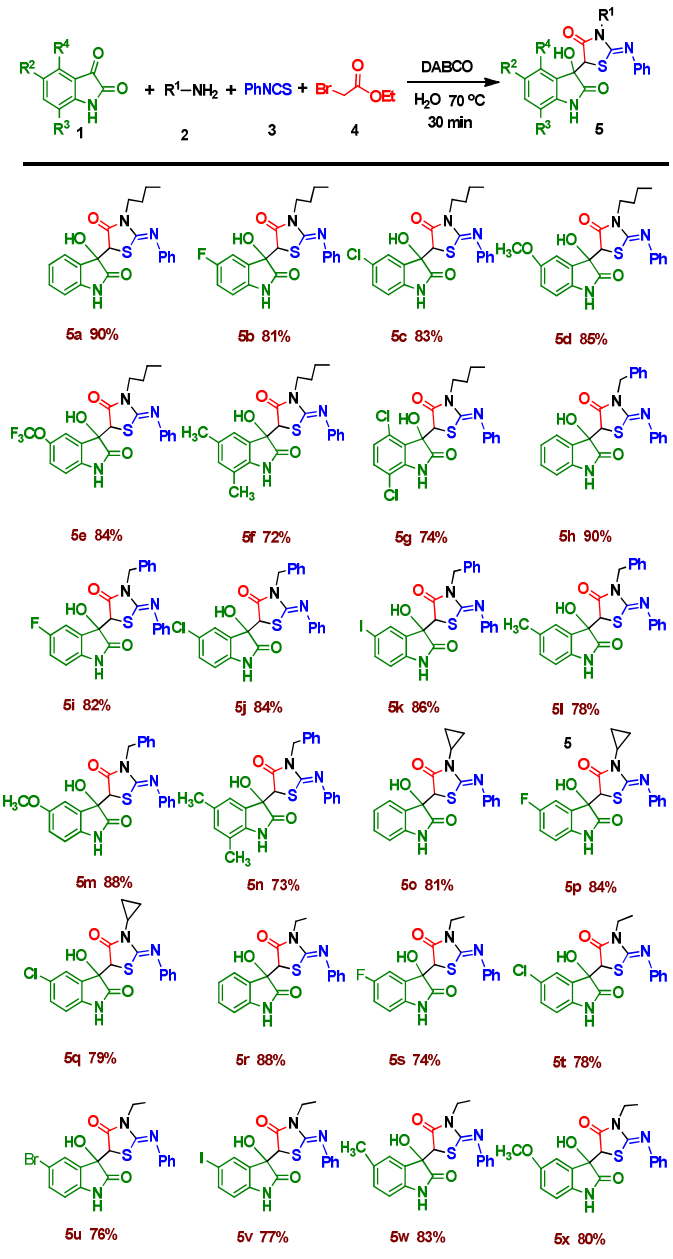
Entry	Catalyst (mol %)	Solvent	Time (h)	Yield[b] [%]
1	–	H_2O	12	–
2	DBU (30)	H_2O	1	55
3	DBU (60)	H_2O	2	50
4	DABCO (10)	H_2O	12	–[c]
5	DABCO (10)	H_2O	1	70
6	**DABCO (30)**	**H_2O**	**0.5**	**90**
7	DABCO (50)	H_2O	1	80
8	DABCO (30)	EtOH	1	65
9	DABCO (30)	MeOH	1	55
10	DABCO (30)	THF	1	30
11	DABCO (30)	CH_3CN	1	35
12	Quinuclidine (30)	H_2O	1	40
13	Urotropine (30)	H_2O	1	35
14	DBN (30)	H_2O	1	50
15	Troger's base (30)	H_2O	1	30
16	Pyridine (30)	H_2O	1	30
17	Piperidine (30)	H_2O	1	25
18	TEA (30)	H_2O	1	30
19	DIPEA (30)	H_2O	1	25
20	KOH (30)	H_2O	1	–
21	K_2CO_3 (30)	H_2O	1	–
22	Cs_2CO_3 (30)	H_2O	1	–
23	MeONa (30)	H_2O	1	–

[a] *Reaction conditions*: isatin **1a** (1 mmol), butylamine **2a** (1 mmol), phenylisothiocyanate **3** (1 mmol) and ethylbromoacetate **4** (1 mmol) base in solvent (5 mL) at rt and 70 °C. [b] isolated yield. [c] at rt conditions.

Further increase in the amount of DBU (30 mol % to 60 mmol %) did not improve the yield of the product (Table 1, entry 3). However, the reaction did not proceed in the absence of catalyst (Table 1, entry 1), which indicated that the use of base catalyst is essential for this MCR. Later, other bases also were tested for this MCR. First, DABCO (10 mol%) was used at room temperature and under heating condition (Table 1, entries 4 and 5 respectively), and the results indicated that DABCO was superior to DBU. It was noticed that there was a maximum increase in the yield (90 %), when the amount of DABCO raised from 10 mol% to 30 mol% in 30 min (Table 1, entry 6). However, further raising the amount of DABCO did not increase in the yield (Table 1, entry 7). Next, quinuclidine,

urotropine, DBN, troger's base, pyridine, piperidine, TEA and DIPEA as a catalyst for this reaction also were examined, but the results were inadequate (Table 1, entries 12−19). In addition, the inorganic bases such as KOH, K_2CO_3, Cs_2CO_3 and MeONa were ineffective for this reaction (Table 1, entries 20 and 23).

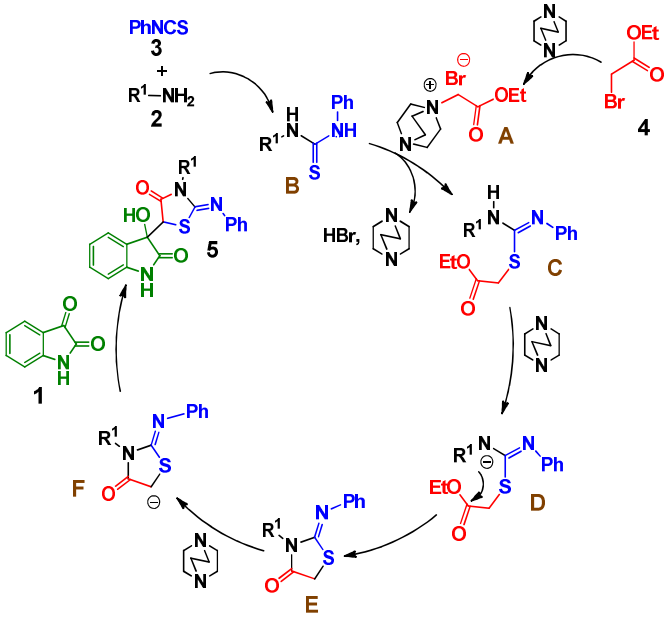
Table 2: Scope of isatins and amines for the synthesis of (Z)-5-(3-hydroxy-2-oxoindolin-3-yl)-2-iminothiazolidin-4-ones[a]



[a] *Reaction conditions*: isatin **1(a-j)** (1 mmol), amine **2(a-d)** (1 mmol), phenylisothiocyanate **3** (1 mmol) and ethylbromoacetate **4** (1 mmol) DABCO (30 mol %) in H_2O (5 mL) at 70 °C and yields are given as an isolated yield. All products **5(a–x)** were characterized by NMR, Mass and IR spectroscopic techniques.

Further to optimize the reaction conditions, the reaction was studied in different solvents. Screening of solvents revealed that H_2O turned out to be suitable solvent, which provided not only a shorter reaction time, but also a higher yield than other tested solvents such as EtOH, MeOH, THF and CH_3CN (Table 1, entries 8−11). Therefore, the reaction conditions of 30 mmol % of DABCO as a catalyst in H_2O at 70 °C were best conditions for the preparation of **5a**.

To make the present protocol general, various isatins **1** and amines **2** were examined under optimized conditions and the results are summarized in Table 2. The reaction of butylamine **2a** and ethylamine **2d** with simple isatin **1a** underwent smoothly in the standard reaction condition to furnish the desired product in a high yield (Table 2, entries **5a** and **5r**). Isatins bearing different substituents on the aromatic ring could also be coupled effectively under this condition. For example 5-halo isatins like 5-fluoro isatin **1b** 5-chloro isatin **1c**, 5-bromo isatin **1d**, and 5-iodo isatin **1e** reacted with amine (**2a**/**2b**/**2c**/**2d**) under standard condition and resulted in moderate yields of product (Table 2, entries **5b**, **5c**, **5i**, **5j**, **5k, 5p**, **5q**, **5s**, **5t**, **5u** and **5v**). Other 5-substituted isatins like 5-(trifluoromethoxy) isatin **1h** reacted smoothly with **2a** to furnish desired product in high yield (Table 2, entry **5e**). The reaction was not only successful with isatins having electron withdrawing substituent but also with isatins bearing electron donating group like 5-methyl isatin **1f** and 5-methoxy isatin **1g** (Table 2, entries **5d**, **5l**, **5m, 5w** and **5x**). As like mono-substituted isatins, di-substituted isatin like 5,7-dimethyl isatin **1i** and 4,7-dichloro isatin **1j** reacted in the same way and afforded comparatively less yield of desired products under standard reaction condition (Table 2, entries **5f**, **5g**, and **5n**). To further expand the scope of the method we were keen to explore cyclic amines in this reaction under the optimized reaction conditions. In this context we performed the reaction of cyclopropylamine **2c** with different substituted isatins under standard reaction conditions and found the formation of desired products in good yield (Table 2, entries **5o-5q**). Moreover, this transformation is clean, easy to work up and all the structurally varied substrates reacted smoothly under the standard reaction conditions to afford their respective products in high purities with good yields (products **5a**–**5x**).



Scheme 2. Putative mechanistic pathway for the formation of (Z)-5-(3-hydroxy-2-oxoindolin-3-yl)-2-iminothiazolidin-4-ones.

A plausible mechanism for this DABCO catalyzed four-componenet reaction proposed and illustrated in Scheme **2**. The formation of product may be explained by the reaction of ethylbromoaectate (**4**) with DABCO which forms the quaternary salt **A**. Later it reacts with sulfur of thiourea derivative **B** (which was *insitu* generated from amine **2** and phenylisothiocyanate **3**) to furnish the intermediate **C** by eliminating HBr and DABCO. Next, the nucleophile of amine group promptly attacked on carbonyl group of ester by proton abstraction by DABCO leading to the five-membered cyclised intermediate **E**. Finally, the nucleophile of **E** which is formed by proton abstraction by DABCO attacked on isatin to furnish the required product (Z)-5-(3-hydroxy-2-oxoindolin-3-yl)-2-iminothiazolidin-4-one **5**. However the stereo chemistry of the product **5** could not be determined because of difficulty in the formation of crystal for X-ray data.

Conclusion:

In summary, we have described a novel and efficient method for the synthesis of (z)-5-(3-hydroxy-2-oxoindolin-3-yl)-2-iminothiazolidin-4-one derivatives from simple, commercially cheap and readily available starting materials. The DABCO catalyzed four-component reaction of isatins, amines, phenylisothiocyanate and ethylbromoacetate proceeds smoothly under metal-free conditions. This novel method has many important features such as, high efficiency, good yields, broad substrate scope and also it involves the formation of four new bonds (2 C-N, 1 C-S, 1 C-C) in a cascade pathway.

Experimental section

General information

Isatins, amines, phenylisothiocyanate, ethylbromoacetate, DABCO and all solvents were purchased from Sigma-Aldrich and Alpha Aesar and used as received without further purification. ^{1}H NMR spectra were recorded at 300 MHz and ^{13}C NMR spectra at 75 MHz spectrometers in DMSO-d_6 or $CDCl_3$+DMSO-d_6. Chemical shifts (d) are reported in parts per million (ppm) relative to residual $CHCl_3$ (^{1}H: δ 7.26 ppm, ^{13}C: δ 77.00 ppm) as an internal reference. Coupling constants (J) are reported in Hertz (Hz) and peak multiplicity abbreviations used as follows: s—singlet, d—doublet, t—triplet, q—quartet, m—multiplet and dd—doublet of doublet. Chemical shifts (δ) are reported relative to TMS (δ 0.0) as an internal standard in ppm. Melting points were measured on a BUCHI melting point machine. IR spectra were recorded on a Thermo Nicolet FT/IR-5700 spectrometer. Mass spectra were recorded using a Waters mass spectrometer. High resolution mass spectra (HRMS) were recorded using an Applied Bio-Sciences HRMS spectrometer at the National Centre for Mass Spectroscopy-IICT.

General procedure for the synthesis of (Z)-3-butyl-5-(3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5a): A mixture of butylamine **2a** (1 mmol), phenylisothiocyanate **3** (1 mmol) and DABCO (30 mol %) in H_2O (5 mL) was stirred for 5 min at room temperature then the ethylbromoacetate **4** (1 mmol) was added and the mixture was stirred at 70 ^{o}C for 10 min. After cooling to room temperature, isatin **1** (1 mmol) was added to the reaction mixture and stirred for 10 min at room temperature. After completion of the reaction (monitored by TLC), the product **5a** was extracted with ethylacetate and dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by column chromatography using ethyl acetate/hexane and the product (Z)-3-butyl-5-(3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one **5a** was characterized by NMR, Mass and IR spectroscopic techniques.

Spectral data for all the synthesized compounds

(Z)-3-butyl-5-(3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino) thiazolidin-4-one (5a): Yield, 90%; Isatin (1 mmol), butylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Yellow solid; Mp 146-148 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.11 (s, 1H), 7.57 (d, *J* = 7.36 Hz, 1H), 7.51 (s, 1H), 7.37 (t, *J* = 7.74 Hz, 2H), 7.24 (t, *J* = 7.74 Hz, 1H), 7.14 (t, *J* = 7.36 Hz, 1H), 7.03-6.93 (m, 2H), 6.86 (d, *J* = 7.74 Hz, 1H), 6.51 (s, 1H), 4.82 (s, 1H), 3.68-3.46 (m, 2H), 1.37-0.84 (m, 4H), 0.75 (t, *J* = 6.98 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 176.8, 171.5, 152.3, 147.7, 141.4, 130.9, 129.2, 126.5, 124.6, 124.5, 123.1, 120.7, 110.9, 76.7, 53.1, 42.9, 28.8, 19.7, 13.6 ppm; IR(KBr): ν = 3316, 2959, 2928, 1725, 1634, 1593, 1408, 1180, 1120, 754 cm^{-1}; MS-ESI: m/z = 396 $[M+1]^+$; HRMS (ESI) calc. $C_{21}H_{22}O_3N_3S$: 396.13764, found: 396.13849.

(Z)-3-butyl-5-(5-fluoro-3-hydroxy-2-oxoindolin-3-yl)-2(phenylimino)thiazolidin-4-one (5b): Yield, 81%; 5-fluoro isatin (1 mmol), butylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Red solid; Mp 176-179 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.93 (s, 1H), 10.25 (s, 1H), 7.55 (s, 1H), 7.44-7.12 (m, 3H), 7.04-6.89 (m, 2H), 6.88-6.73 (m, 2H), 4.83 (s, 1H), 3.69-3.47 (m, 2H), 1.36-0.91 (m, 4H), 0.77 (t, *J* = 7.17 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 183.6, 176.3, 159.0, 152.8, 147.6, 146.5, 138.0, 128.7, 124.5, 124.3, 124.0, 120.2, 113.3, 75.2, 55.1, 41.7, 28.2, 19.0, 13.1 ppm; IR(KBr): ν = 3262, 2930, 2860, 1728, 1633, 1487, 1397, 1192, 1145, 739, 694 cm^{-1}; MS-ESI: m/z = 414 $[M+1]^+$; HRMS (ESI) calc. $C_{21}H_{21}O_3N_3FS$: 414.12822, found: 414.12887.

(Z)-3-butyl-5-(5-chloro-3-hydroxy-2-oxoindolin-3-yl)-2(phenylimino)thiazolidin-4-one (5c): Yield, 83%; 5-chloro isatin (1 mmol), butylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Pale red solid; Mp 184-186 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.16 (s, 1H), 7.58 (s, 1H), 7.47-7.33 (m, 2H), 7.27-7.13 (m, 2H), 6.99 (d, *J* = 7.55 Hz, 1H), 6.82 (d, *J* = 8.30 Hz, 1H), 6.62 (s, 1H), 4.80 (s, 1H), 3.70-3.49 (m, 2H), 1.38-1.20 (m, 2H), 1.15-0.92 (m, 2H), 0.79 (t, *J* = 6.98 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 176.3, 169.7, 153.1, 147.9, 140.7, 129.8, 128.9, 128.1, 126.8, 124.7, 124.2, 120.4, 111.2, 75.3, 55.2, 42.0, 28.4, 19.2, 13.3 ppm; IR(KBr): ν = 3275, 2956, 2872, 1736, 1638, 1594, 1397, 1181, 1129, 698 cm^{-1}; MS-ESI: m/z = 430 $[M+1]^+$; HRMS (ESI) calc. $C_{21}H_{21}O_3N_3ClS$: 430.09867, found: 430.09928.

(Z)-3-butyl-5-(3-hydroxy-5-methoxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5d): Yield, 85%; 5-methoxy isatin (1 mmol), butylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Block solid; Mp 138-140 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.19 (s, 1H), 7.38 (t, *J* = 7.97 Hz, 3H), 7.23-7.12 (m, 2H), 7.01-6.94 (m, 2H), 6.82-6.73 (m, 3H), 4.80 (s, 1H), 3.75 (s, 3H), 3.64-3.43 (m, 2H), 1.12-0.81 (m, 4H), 0.74 (t, *J* = 7.15 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.7, 167.9, 153.3, 152.1, 146.6, 134.3, 127.6, 126.4, 122.7, 119.1, 113.4, 109.6, 108.8, 73.7, 54.3, 53.8, 40.2, 27.0, 17.7, 12.0 ppm; IR(KBr): ν = 3243, 2957, 2873, 1722, 1705, 1633, 1592, 1487, 1391, 1202, 1184 cm^{-1}; MS-ESI: m/z = 426 $[M+1]^+$; HRMS (ESI) calc. $C_{22}H_{24}O_4N_3S$: 426.14820, found: 426.14872.

(Z)-3-butyl-5-(3-hydroxy-2-oxo-5-(trifluoromethoxy)indolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5e): Yield, 84%; 5-(trifluoromethoxy) isatin (1 mmol), butylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and

DABCO (30 mol %) in H_2O (5 mL); Yellow solid; Mp 193-195 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 8.18 (s, 1H), 7.39 (s, 1H), 7.33 (t, *J* = 8.08 Hz, 2H), 7.18-7.12 (m, 2H), 6.91 (d, *J* = 8.54 Hz, 2H), 6.86 (d, *J* = 8.08 Hz, 1H), 4.67 (s, 1H), 3.81-3.66 (m, 2H), 1.33-1.15 (m, 4H), 0.86 (t, *J* = 7.47 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 176.0, 168.9, 152.4, 147.5, 142.9, 141.0, 128.5, 128.3, 127.5, 123.7, 122.7, 120.0, 117.8, 110.1, 74.7, 55.3, 41.5, 27.9, 18.7, 12.7 ppm; IR(KBr): ν = 3265, 2928, 2856, 1733, 1712, 1638, 1595, 1398, 1268, 1188, 1158, 695 cm^{-1}; MS-ESI: m/z = 480 $[M+1]^+$; HRMS (ESI) calc. $C_{22}H_{21}O_4N_3F_3S$: 480.11994, found: 480.12021.

(Z)-3-butyl-5-(3-hydroxy-5,7-dimethyl-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5f): Yield, 72%; 5,7-dimethyl isatin (1 mmol), butylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Brown solid; Mp 226-228 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.42 (s, 1H), 7.40 (t, *J* = 7.78 Hz, 2H), 7.21-7.14 (m, 2H), 6.95 (d, *J* = 7.47 Hz, 2H), 6.87 (s, 1H), 6.68 (s, 1H), 4.74 (s, 1H), 3.57-3.50 (m, 2H), 2.25 (s, 3H), 2.16 (s, 3H), 1.17-1.04 (m, 1H), 0.98-0.75 (m, 3H), 0.70 (t, *J* = 7.17 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 176.1, 169.0, 153.0, 147.4, 137.7, 131.1, 129.9, 128.2, 125.6, 123.3, 121.6, 119.8, 118.3, 74.7, 54.8, 41.1, 27.7, 19.9, 18.4, 15.4, 12.7 ppm; IR(KBr): ν = 3297, 2954, 1715, 1698, 1634, 1596, 1486, 1398, 1155 cm^{-1}; MS-ESI: m/z = 424 $[M+1]^+$; HRMS (ESI) calc. $C_{23}H_{26}O_3N_3S$: 424.16894, found: 424.16918.

(Z)-3-butyl-5-(4,7-dichloro-3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5g): Yield, 74%; 4,7-dichloro isatin (1 mmol), butylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Brown solid; Mp 136-138 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.27 (s, 1H), 7.37-7.19 (m, 3H), 7.14-6.83 (m, 4H), 4.82 (s, 1H), 3.72-3.64 (m, 2H), 1.21-0.98 (m, 4H), 0.94 (t, *J* = 6.98 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 173.8, 170.3, 150.5, 146.5, 141.4, 130.6, 127.9, 124.4, 123.3, 122.8, 119.9, 119.6, 113.0, 77.7, 51.4, 44.9, 27.7, 18.6, 12.6 ppm; IR(KBr): ν = 3406, 2930, 2873, 1738, 1634, 1613, 1594, 1465, 1388, 1344, 1158, 1057, 775 cm^{-1}; MS-ESI: m/z = 464 $[M+1]^+$; HRMS (ESI) calc. $C_{21}H_{20}O_3N_3Cl_2S$: 464.05969, found: 464.06090.

(Z)-3-benzyl-5-(3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5h): Yield, 90%; Isatin (1 mmol), benzylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Pale yellow solid; Mp 186-188 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.08 (s, 1H), 7.55 (d, *J* = 7.36 Hz, 1H), 7.39-7.30 (m, 3H), 7.18-7.07 (m, 4H), 6.97-6.81 (m, 5H), 6.51 (s, 1H), 4.93 (s, 1H), 4.77 (d, *J* = 5.09 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.8, 168.1, 151.5, 146.3, 141.3, 133.7, 128.7, 127.6, 127.3, 126.5, 125.2, 125.0, 123.2, 122.8, 120.0, 119.2, 108.6, 73.3, 54.5, 43.6 ppm; IR(KBr): ν = 3292, 2926, 1728, 1643, 1470, 1399, 1333, 1173, 1020, 748 cm^{-1}; MS-ESI: m/z = 430 $[M+1]^+$; HRMS (ESI) calc. $C_{24}H_{20}O_3N_3S$: 430.12199, found: 430.12215.

(Z)-3-benzyl-5-(5-fluoro-3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5i): Yield, 82%; 5-fluoro isatin (1 mmol), benzylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 202-204 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.37 (s, 1H), 7.42-7.33 (m, 2H), 7.26 (dd, *J* = 2.64, 2.64 Hz, 2H), 7.20-7.09 (m, 3H), 6.97-6.85 (m, 6H), 4.91 (s, 1H), 4.75 (d, *J* = 1.70 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.8, 167.9, 157.9, 154.7, 151.4, 146.4, 137.3, 133.8, 127.7, 126.6, 125.6, 125.5, 123.0, 119.2, 115.2, 114.9, 109.3, 73.6, 54.4, 43.8 ppm; IR(KBr): ν = 3291, 2936, 1727, 1704, 1644, 1590, 1484, 1402, 1333, 1246, 1188, 1088, 817, 695 cm^{-1}; MS-ESI: m/z = 448 $[M+1]^+$; HRMS (ESI) calc. $C_{24}H_{19}O_3N_3FS$: 448.11257, found: 448.11293.

(Z)-3-benzyl-5-(5-chloro-3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5j): Yield, 84%; 5-chloro isatin (1 mmol), benzylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 209-211 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.46 (s, 1H), 7.53 (d, *J* = 2.07 Hz, 1H), 7.41-7.34 (m, 2H), 7.19-7.11 (m, 4H), 6.97-6.89 (m, 3H), 6.87-6.82 (m, 2H), 6.75-6.69 (m, 1H), 4.89 (s, 1H), 4.75 (d, *J* = 10.57 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.0, 167.5, 151.3, 146.1, 139.7, 133.4, 128.3, 127.4, 126.9, 126.3, 125.1, 124.6, 124.0, 123.0, 122.6, 118.7, 109.5, 72.9, 54.1, 43.4 ppm; IR(KBr): ν = 3278, 2923, 1732, 1703, 1646, 1589, 1479, 1401, 1174, 1097, 1022, 816, 695 cm^{-1}; MS-ESI: m/z = 464 $[M+1]^+$; HRMS (ESI) calc. $C_{24}H_{19}O_3N_3ClS$: 464.08302, found: 464.08364.

(Z)-3-benzyl-5-(3-hydroxy-5-iodo-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5k): Yield, 86%; 5-iodo isatin (1 mmol), benzylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 215-217 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.19 (s, 1H), 7.48-7.44 (m, 1H), 7.42-7.34 (m, 2H), 7.22-7.12 (m, 4H), 7.02-6.81 (m, 4H), 6.73-6.64 (m, 1H), 6.61-6.54 (m, 1H), 4.87 (s, 1H), 4.77 (d, *J* = 9.63 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.4, 168.0, 151.9, 146.8, 141.2, 137.4, 133.8, 132.2, 127.9, 127.8, 127.0, 125.7, 125.4, 123.1, 119.3, 111.1, 82.6, 73.6, 54.8, 44.2 ppm; IR(KBr): ν = 3281, 2920, 1730, 1700, 1646, 1589, 1404, 1332, 1174, 1093, 1023, 815, 694 cm^{-1}; MS-ESI: m/z = 556 $[M+1]^+$; HRMS (ESI) calc. $C_{24}H_{19}O_3N_3IS$: 556.01239, found: 556.01345.

(Z)-3-benzyl-5-(3-hydroxy-5-methyl-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5l): Yield, 78%; 5-methyl isatin (1 mmol), benzylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 195-197 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 9.74 (s, 1H), 7.41-7.29 (m, 4H), 7.23-7.09 (m, 4H), 6.97-6.89 (m, 3H), 6.71 (d, *J* = 7.93 Hz, 1H), 6.26 (s, 1H), 4.88 (s, 1H), 4.79 (d, *J* = 11.08 Hz, 2H), 2.17 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.4, 167.8, 151.6, 146.2, 138.5, 133.5, 128.7, 128.6, 127.4, 126.2, 125.2, 125.0, 124.7, 123.6, 122.5, 118.8, 107.9, 73.1, 54.3, 43.4, 19.1 ppm; IR(KBr): ν = 3288, 2919, 1728, 1644, 1589, 1489, 1398, 1362, 1330, 1201, 1155, 1087, 813, 695 cm^{-1}; MS-ESI: m/z = 444 $[M+1]^+$; HRMS (ESI) calc. $C_{25}H_{22}O_3N_3S$: 444.13764, found: 444.13795.

(Z)-3-benzyl-5-(3-hydroxy-5-methoxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5m): Yield, 88%; 5-methoxy isatin (1 mmol), benzylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Brown solid; Mp 105-107 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.18 (s, 1H), 7.38-7.31 (m, 3H), 7.18-7.08 (m, 4H), 6.91 (d, *J* = 7.17 Hz, 2H), 6.83-6.72 (m, 4H), 4.93 (s, 1H), 4.75 (d, *J* = 8.49 Hz, 2H), 3.58 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.7, 168.0, 153.2, 151.6, 146.3, 134.4, 133.8, 127.6, 127.4, 126.5, 126.3, 125.3, 122.8, 119.1, 114.2, 109.3, 109.0, 73.6, 54.5, 53.7, 43.7 ppm; IR(KBr): ν = 3309, 2928, 1725, 1633, 1590, 1488, 1386, 1204, 1158, 1028, 818, 695 cm^{-1}; MS-ESI: m/z = 460 $[M+1]^+$; HRMS (ESI) calc. $C_{25}H_{22}O_4N_3S$: 460.13255, found: 460.13335.

(Z)-3-benzyl-5-(3-hydroxy-5,7-dimethyl-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5n): Yield, 73%; 5,7-dimethyl isatin (1 mmol), benzylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 238-240 °C; ^{1}H NMR (300 MHz,

$CDCl_3$+DMSO-d_6): δ 10.33 (s, 1H), 7.40-7.34 (m, 3H), 7.20-7.06 (m, 3H), 6.91 (d, *J* = 7.36 Hz, 2H), 6.84 (s, 1H), 6.75 (d, *J* = 6.98 Hz, 2H), 6.66 (s, 1H), 4.87 (s, 1H), 4.72 (s, 2H), 2.16 (s, 3H), 2.15 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 175.5, 168.2, 152.0, 146.7, 137.3, 133.9, 130.8, 129.2, 127.8, 127.6, 126.5, 125.5, 125.1, 122.9, 121.3, 119.3, 117.6, 73.9, 54.7, 43.9, 19.4, 15.0 ppm; IR(KBr): ν = 3314, 2920, 1717, 1700, 1637, 1593, 1485, 1398, 1200, 1153, 1073, 695 cm^{-1}; MS-ESI: m/z = 458 $[M+1]^+$; HRMS (ESI) calc. $C_{26}H_{24}O_3N_3S$: 458.15329, found: 458.15378.

(Z)-3-cyclopropyl-5-(3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5o): Yield, 81%; Isatin (1 mmol), cyclopropylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 190-192 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.43 (s, 1H), 7.71 (d, *J* = 7.36 Hz, 1H), 7.36-7.29 (m, 4H), 7.04-6.89 (m, 3H), 6.69-6.64 (m, 1H), 5.11 (s, 1H), 2.34-2.21 (m, 1H), 1.72-0.30 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 175.1, 168.3, 141.6, 131.3, 129.4, 129.3, 127.9, 126.0, 125.6, 123.3, 120.7, 120.5, 109.4, 74.3, 56.0, 22.3, 4.8, 4.1 ppm; IR(KBr): ν = 3270, 2931, 1720, 1695, 1621, 1471, 1371, 1185, 1145, 758 cm^{-1}; MS-ESI: m/z = 380 $[M+1]^+$; HRMS (ESI) calc. $C_{20}H_{18}O_3N_3S$: 380.09912, found: 380.09983.

(Z)-3-cyclopropyl-5-(5-fluoro-3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5p): Yield, 84%; 5-fluoro isatin (1 mmol), cyclopropylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 142-144 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.36 (s, 1H), 7.57 (s, 1H), 7.49-7.42 (m, 1H), 7.40-7.34 (m, 1H), 7.30-7.24 (m, 1H), 7.05-6.93 (m, 2H), 6.89-6.79 (m, 2H), 4.90 (s, 1H), 2.39-2.30 (m, 1H), 1.06-0.41 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 175.3, 169.4, 137.7, 131.4, 128.2, 126.1, 115.9, 115.7, 111.5, 111.2, 111.0, 110.4, 110.2, 74.6, 55.1, 22.7, 5.0, 4.4 ppm; IR(KBr): ν = 3277, 2927, 1722, 1696, 1486, 1380, 1192, 1144, 822 cm^{-1}; MS-ESI: m/z = 398 $[M+1]^+$; HRMS (ESI) calc. $C_{20}H_{17}O_3N_3FS$: 398.02354, found: 398.02358.

(Z)-5-(5-chloro-3-hydroxy-2-oxoindolin-3-yl)-3-cyclopropyl-2-(phenylimino)thiazolidin-4-one (5q): Yield, 79%; 5-chloro isatin (1 mmol), cyclopropylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 149-151 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.36 (s, 1H), 7.54-7.36 (m, 4H), 7.32-7.18 (m, 2H), 6.89-6.79 (m, 2H), 4.89 (s, 1H), 2.42-2.33 (m, 1H), 1.04-0.45 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 175.0, 169.3, 140.3, 131.4, 129.4, 129.3, 128.2, 127.4, 126.1, 125.6, 123.6, 123.4, 110.6, 74.3, 55.1, 22.6, 5.1, 4.4 ppm; IR(KBr): ν = 3281, 1722, 1695, 1620, 1476, 1380, 1181, 823 cm^{-1}; MS-ESI: m/z = 414 $[M+1]^+$; HRMS (ESI) calc. $C_{20}H_{17}O_3N_3ClS$: 414.01276, found: 414.01321.

(Z)-3-ethyl-5-(3-hydroxy-2-oxoindolin-3-yl)-2-(phenylimino)thiaz-olidin-4-one (5r): Yield, 88%; Isatin (1 mmol), ethylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 147-149 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.22 (s, 1H), 7.59 (d, *J* = 7.36 Hz, 1H), 7.51 (s, 1H), 7.37-7.18 (m, 2H), 7.07-6.82 (m, 3H), 6.81-6.61 (m, 2H), 4.97 (s, 1H), 3.38 (q, *J* = 7.36 Hz, 2H), 0.67 (t, *J* = 7.36 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.4, 169.1, 167.9, 141.0, 128.8, 128.6, 127.3, 125.5, 125.1, 122.6, 120.0, 119.9, 108.4, 73.3, 55.5, 34.1, 10.2 ppm; IR(KBr): ν = 3280, 2934, 1719, 1682, 1622, 1471, 1342, 1222, 1183, 1090, 755 cm^{-1}; MS-ESI: m/z = 368 $[M+1]^+$; HRMS (ESI) calc. $C_{19}H_{18}O_3N_3S$: 368.14319, found: 368.14381.

(Z)-3-ethyl-5-(5-fluoro-3-hydroxy-2-oxoindolin-3-yl)-2-(phenylim-ino)thiazolidin-4-one (5s): Yield, 74%; 5-fluoro isatin (1 mmol), ethylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 164-166 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.41 (s, 1H), 7.66-7.43 (m, 1H), 7.40-7.30 (m, 2H), 7.08-6.75 (m, 5H), 4.99 (s, 1H), 3.40 (q, *J* = 7.15 Hz, 2H), 0.70 (t, *J* = 7.15 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 175.4, 169.8, 168.7, 158.8, 137.8, 128.2, 127.1, 126.1, 115.9, 115.6, 111.5, 111.2, 110.2, 74.5, 56.0, 35.2, 11.1 ppm; IR(KBr): ν = 3259, 2930, 1722, 1684, 1488, 1392, 1340, 1193, 1148, 822 cm^{-1}; MS-ESI: m/z = 386 $[M+1]^+$; HRMS (ESI) calc. $C_{19}H_{17}O_3N_3FS$: 386.01211, found: 386.01295.

(Z)-5-(5-chloro-3-hydroxy-2-oxoindolin-3-yl)-3-ethyl-2-(phenyli- mino)thiazolidin-4-one (5t): Yield, 78%; 5-chloro isatin (1 mmol), ethylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 169-171 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.57 (s, 1H), 7.70 (s, 1H), 7.54 (d, *J* = 2.07 Hz, 1H), 7.49-7.34 (m, 1H), 7.32-7.13 (m, 2H), 7.08-6.77 (m, 3H), 4.98 (s, 1H), 3.39 (q, *J* = 7.17 Hz, 2H), 0.68 (t, *J* = 7.17 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.7, 169.3, 168.3, 140.2, 129.0, 128.8, 127.8, 127.5, 127.3, 125.8, 125.2, 123.3, 110.2, 73.8, 55.7, 34.8, 10.6 ppm; IR(KBr): ν = 3280, 2934, 1717, 1685, 1480, 1337, 1180, 1104, 824 cm^{-1}; MS-ESI: m/z = 402 $[M+1]^+$; HRMS (ESI) calc. $C_{19}H_{17}O_3N_3ClS$: 402.13492, found: 402.13512.

(Z)-5-(5-bromo-3-hydroxy-2-oxoindolin-3-yl)-3-ethyl-2-(phenylimino)thiazolidin-4-one (5u): Yield, 76%; 5-bromo isatin (1 mmol), ethylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Pale yellow solid; Mp 190-192 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.62 (s, 1H), 7.82-7.54 (m, 2H), 7.52-7.31 (m, 2H), 7.29-7.01 (m, 2H), 6.95-6.72 (m, 2H), 4.97 (s, 1H), 3.37 (q, *J* = 7.17 Hz, 2H), 0.66 (t, *J* = 7.17 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.2, 169.0, 168.0, 140.4, 131.6, 131.4, 127.6, 127.5, 125.6, 112.1, 110.7, 110.5, 108.6, 73.4, 55.4, 34.4, 10.3 ppm; IR(KBr): ν = 3278, 2936, 1717, 1684, 1618, 1476, 1337, 1221, 1178, 1100, 822 cm^{-1}; MS-ESI: m/z = 446 $[M]^+$, 448 $[M+2]^+$; HRMS (ESI) calc. $C_{19}H_{17}O_3N_3BrS$: 446.08519, found: 446.08469.

(Z)-3-ethyl-5-(3-hydroxy-5-iodo-2-oxoindolin-3-yl)-2-(phenylimino) thiazolidin-4-one (5v): Yield, 77%; 5-iodo isatin (1 mmol), ethylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Brown solid; Mp 199-201 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.67 (s, 1H), 8.04-7.61 (m, 2H), 7.58-7.33 (m, 2H), 7.27-6.97 (m, 2H), 6.83-6.56 (m, 2H), 4.96 (s, 1H), 3.35 (q, *J* = 7.17 Hz, 2H), 0.63 (t, *J* = 7.17 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.1, 169.1, 168.1, 141.1, 137.6, 137.4, 131.3, 127.9, 127.7, 125.8, 111.4, 111.1, 82.3, 73.4, 55.6, 34.6, 10.5 ppm; IR(KBr): ν = 3295, 2974, 1715, 1694, 1467, 1378, 1332, 1222, 1175, 1093, 828 cm^{-1}; MS-ESI: m/z = 493 $[M+1]^+$; HRMS (ESI) calc. $C_{19}H_{17}O_3N_3IS$: 493.21462, found: 493.21493.

(Z)-3-ethyl-5-(3-hydroxy-5-methyl-2-oxoindolin-3-yl)-2-(phenyl- imino)thiazolidin-4-one (5w): Yield, 83%; 5-methyl isatin (1 mmol), ethylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); Brown solid; Mp 167-169 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.35 (s, 1H), 7.84 (s, 1H), 7.54-7.28 (m, 2H), 7.23-6.95 (m, 2H), 6.92-6.59 (m, 3H), 4.94 (s, 1H), 3.34 (q, *J* = 7.17 Hz, 2H), 2.24 (s, 3H), 0.60 (t, *J* = 7.17 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.5, 169.3, 168.0, 138.6, 129.1, 128.8, 127.4, 127.2, 125.6, 125.2, 123.2, 108.5, 108.3, 73.5, 55.5, 34.2, 19.2, 10.1 ppm; IR(KBr): ν = 3296, 2952, 1712, 1674, 1628, 1581, 1472, 1318, 1123 cm^{-1}; MS-ESI: m/z = 382 $[M+1]^+$; HRMS (ESI) calc. $C_{20}H_{20}O_3N_3S$: 382.11456, found: 382.11501.

(Z)-3-ethyl-5-(3-hydroxy-5-methoxy-2-oxoindolin-3-yl)-2-(phenylimino)thiazolidin-4-one (5x): Yield, 80%; 5-methoxy isatin (1 mmol), ethylamine (1 mmol), phenylisothiocyanate (1 mmol), ethylbromoacetate (1 mmol) and DABCO (30 mol %) in H_2O (5 mL); White solid; Mp 133-135 °C; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6): δ 10.30 (s, 1H), 7.41-7.14 (m, 3H), 7.05-6.65 (m, 5H), 4.95 (s, 1H), 3.70 (s, 3H), 3.34 (q, J = 7.17 Hz, 2H), 0.62 (t, J = 7.17 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6): δ 174.1, 169.1, 167.7, 167.5, 153.0, 134.1, 134.0, 127.2, 126.1, 125.4, 113.3, 109.2, 108.8, 73.4, 55.3, 53.7, 34.0, 10.0 ppm; IR(KBr): ν = 3258, 2934, 1721, 1683, 1493, 1341, 1299, 1209, 1157, 1090, 887 cm^{-1}; MS-ESI: m/z = 398 $[M+1]^+$; HRMS (ESI) calc. $C_{20}H_{20}O_4N_3S$: 398.11568, found: 398.11591.

Acknowledgment

B M B, G S K and A S thank CSIR-UGC for the award of a fellowship and Dr. Ahmed Kamal, Outstanding scientist and Head of MCP Division for his support and encouragement.

The authors thank CSIR, New Delhi for financial support as part of XII five year plan programme under title ACT (CSC-0301).

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DABCO-Catalyzed consecutive one pot four-component protocol for the synthesis of a novel class of (z)-5-(3-hydroxy-2-oxoindolin-3-yl)-2-iminothiazolidin-4-ones

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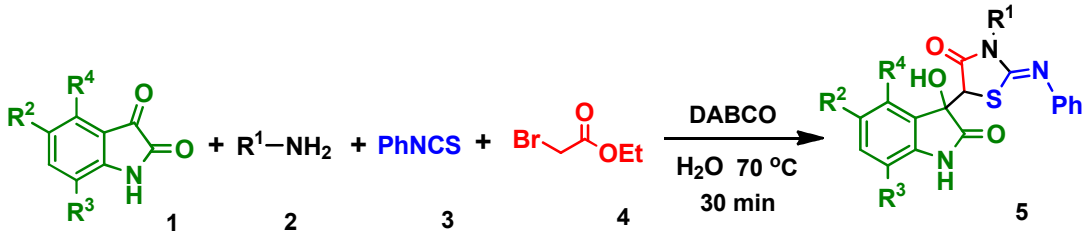

1 2 3 4 5

R^1 = Butyl, Benzyl, Cyclopropyl, Ethyl; R^2 = H, F, Cl, Br, I, CH_3, OCH_3, OCF_3, R^3 = H, Cl, CH_3; R^4 = H, Cl.